

chain nodes :

13 14 17 18 19 20

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12

chain bonds :

3-13 6-12 13-14 14-17 14-18 18-19 18-20

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12

exact/norm bonds :

1-2 1-6 2-3 3-4 3-13 4-5 5-6 6-12 14-17 18-19 18-20

exact bonds :

13-14 14-18

normalized bonds :

7-8 7-12 8-9 9-10 10-11 11-12

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 14:CLASS 17:Atom 18:CLASS 19:CLASS 20:CLASS

10/049795

=> s l1

SAMPLE SEARCH INITIATED 17:54:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1232 TO ITERATE

81.2% PROCESSED 1000 ITERATIONS 4 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 22535 TO 26745
PROJECTED ANSWERS: 4 TO 231

L2 4 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 17:54:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 24706 TO ITERATE

100.0% PROCESSED 24706 ITERATIONS 62 ANSWERS
SEARCH TIME: 00.00.01

L3 62 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.42	156.26

FILE 'CAPLUS' ENTERED AT 17:54:54 ON 15 APR 2004
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FILE COVERS 1907 - 15 Apr 2004 VOL 140 ISS 16
FILE LAST UPDATED: 14 Apr 2004 (20040414/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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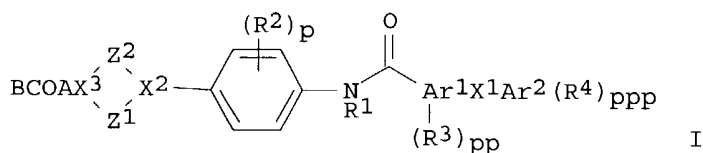
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=> d l4 1-21 bib abs hitstr

10/049795

L4 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:185098 CAPLUS
DN 136:247608
TI Preparation of piperidinyl-, piperazinyl-, and
homopiperazinylpolyarylcaboxamides as lipid lowering agents
IN Meerpoel, Lieven; Roevens, Peter Walter Maria; Backx, Leo Jacobus Jozef;
Van der Veken, Louis Jozef Elisabeth; Viellevoe, Marcel
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002020501	A2	20020314	WO 2001-EP9926	20010827
	WO 2002020501	A3	20020627		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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	EP 1317431	A2	20030611	EP 2001-978313	20010827
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	BR 2001014045	A	20030701	BR 2001-14045	20010827
	JP 2004508361	T2	20040318	JP 2002-525123	20010827
	BG 107581	A	20031128	BG 2003-107581	20030221
	US 2004014971	A1	20040122	US 2003-363665	20030228
	NO 2003001001	A	20030304	NO 2003-1001	20030304
	HR 2003000156	A1	20030430	HR 2003-156	20030304
PRAI	EP 2000-203067	A	20000904		
	WO 2001-EP9926	W	20010827		
OS	MARPAT 136:247608				
GI					



AB Title compds. [I; Z1 = (CH2)n, CH2CH2O; n = 1-3; Z2 = (CH2)m; m = 1, 2; X1 = O, CH2, CO, NH, CH2O, CH2S, bond; X2, X3 = CH, N, C; R1 = H, alkyl; Ar1, Ar2 = (substituted) Ph, naphthalenyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, triazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, pyrrolyl, furyl, thienyl; R2, R3 = alkyl, alkoxy, halo, CF3; R4 = alkyl, alkoxy, halo, OH, SH, cyano, NO2, alkylthio, polyhaloalkyl, amino, alkylamino, dialkylamino; p, pp = 0-2; ppp = 0-3; X1, R4 taken together with Ar1 and Ar2 to which they are attached = fluoren-1-yl, fluoren-4-yl; A = alkanediyl substituted with 1-2 aryl, heteroaryl, cycloalkyl; when X3 = CH, A may also = N substituted with H,

alkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, cycloalkyl; B = H, alkyl, aralkyl, heteroarylalkyl, (substituted) aryl, heteroaryl, etc.], and N-oxides thereof, were prepared. Thus, 4'-trifluoromethylbiphenyl-2-carboxylic acid was stirred 2 h with (COCl)₂ in CH₂Cl₂ containing DMF; the resulting mixture was added to a mixture prepared from 4-(4-aminophenyl)- α -Ph-N-(2,2,2-trifluoroethyl)-1-piperazineacetamide (preparation given) and Et₃N in CH₂Cl₂ under ice/salt cooling followed by stirring and reflux for 2 days to give N-[4-[4-[2-oxo-1-phenyl-2-[(2,2,2-trifluoroethyl)amino]ethyl]-1-piperazinyl]phenyl]-4'-(trifluoromethyl)[1,1'-biphenyl]-2-carboxamide. The latter inhibited microsomal triglyceride transfer protein (MTP) activity with pIC₅₀ = 7.864.

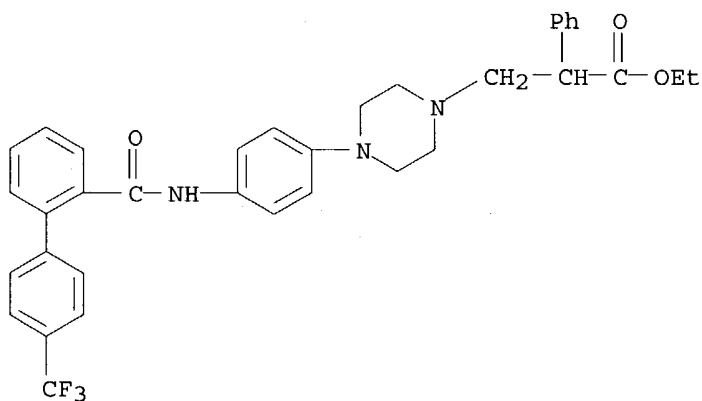
IT 403987-37-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidinyl-, piperazinyl-, and homopiperazinylpolyarylcarboxamides as lipid lowering agents)

RN 403987-37-1 CAPLUS

CN 1-Piperazinepropanoic acid, α -phenyl-4-[4-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl]carbonyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT 403987-75-7P

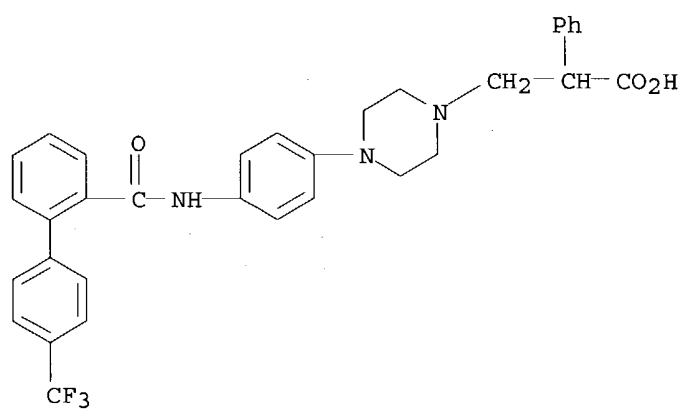
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of piperidinyl-, piperazinyl-, and homopiperazinylpolyarylcarboxamides as lipid lowering agents)

RN 403987-75-7 CAPLUS

CN 1-Piperazinepropanoic acid, α -phenyl-4-[4-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl]carbonyl]amino]phenyl]- (9CI) (CA INDEX NAME)

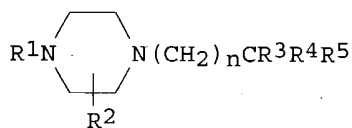
10/049795



10/049795

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:136796 CAPLUS
DN 134:193445
TI Preparation of arylpiperazinylpentanoates and -hexanoates as microsomal triglyceride transfer protein inhibitors.
IN Lehmann-Lintz, Thorsten; Heckel, Armin; Thomas, Leo; Mark, Michael
PA Boehringer Ingelheim Pharma KG, Germany
SO Ger. Offen., 24 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19939745	A1	20010222	DE 1999-19939745	19990821
	WO 2001014355	A1	20010301	WO 2000-EP7976	20000816
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PRAI	DE 1999-19939516	A	19990820		
	DE 1999-19939745	A	19990821		
	WO 2000-EP7976	W	20000816		
OS	MARPAT 134:193445				
GI					



AB Title compds. [I; R₁ = (substituted) Ph; R₂ = H, alkyl; R₃ = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, Ph, naphthyl, heteroaryl; R₄ = (substituted) Ph, naphthyl, heteroaryl; R₅ = CO₂H, (substituted) alkoxy carbonyl, cycloalkoxy carbonyl, etc.; n = 3-5], were prepared as MTP inhibitors for reduction of plasma concentration of atherogenic lipoproteins (no data). Thus, 1-(4-nitrophenyl)piperazine, Me 5-bromo-2-methyl-2-phenylpentanoate, H₂O and K₂CO₃ in MeCN were stirred for 6 h at 60° to give Me 2-methyl-2-phenyl-5-[4-(4-nitrophenyl)piperazin-1-yl]pentanoate, which was hydrogenated over Pd/C in EtOAc/MeOH to give 91.7% Me 2-methyl-2-phenyl-5-[4-(4-aminophenyl)piperazin-1-yl]pentanoate.

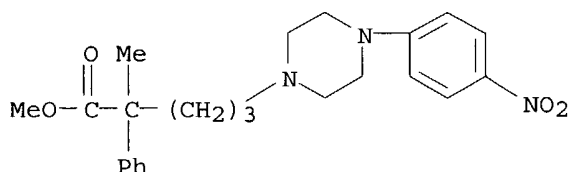
IT 327030-25-1P 327030-26-2P 327030-33-1P
327030-35-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

10/049795

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of arylpiperazinylpentanoates and -hexanoates as microsomal triglyceride transfer protein inhibitors)

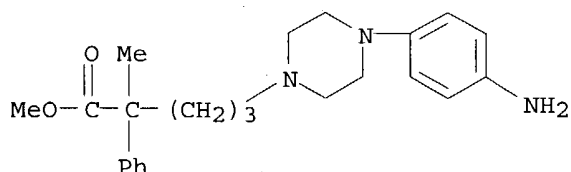
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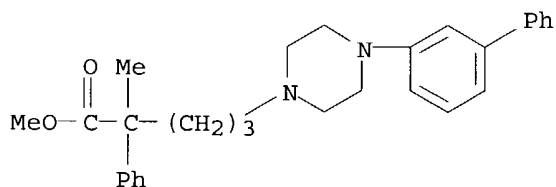
RN 327030-26-2 CAPLUS

CN 1-Piperazinepentanoic acid, 4-(4-aminophenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



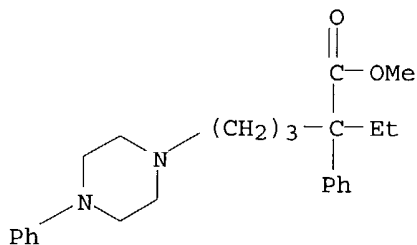
RN 327030-33-1 CAPLUS

CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-3-yl- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-35-3 CAPLUS

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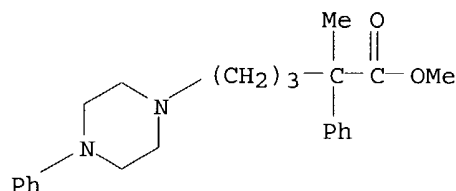
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327030-16-0P 327030-17-1P 327030-18-2P
327030-19-3P 327030-20-6P 327030-21-7P
327030-22-8P 327030-23-9P 327030-24-0P
327030-27-3P 327030-28-4P 327030-29-5P
327030-30-8P 327030-31-9P 327030-36-4P
327030-37-5P 327030-38-6P 327030-42-2P
327030-43-3P 327030-46-6P 327030-47-7P
327030-48-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylpiperazinylpentanoates and -hexanoates as microsomal triglyceride transfer protein inhibitors)

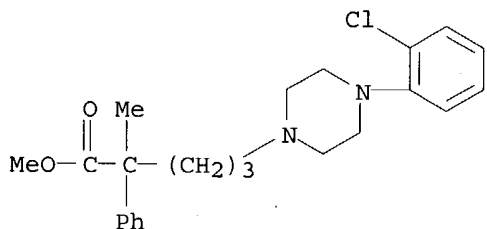
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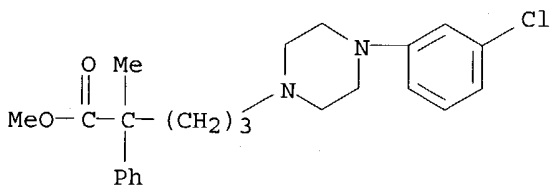
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RN 327030-09-1 CAPLUS

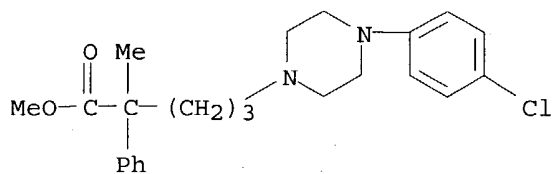
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10/049795

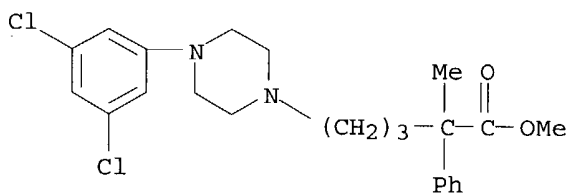
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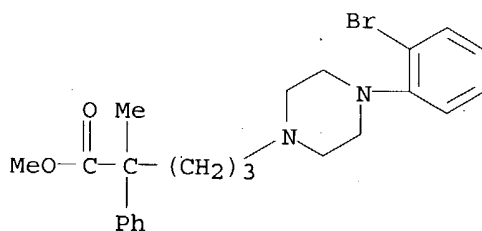
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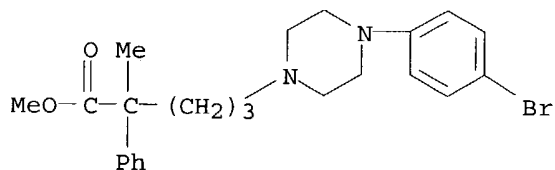
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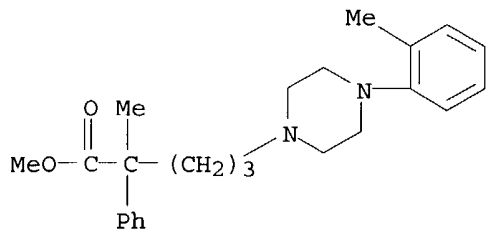
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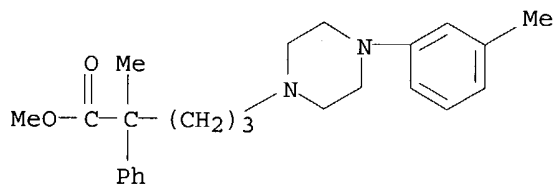
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10/049795



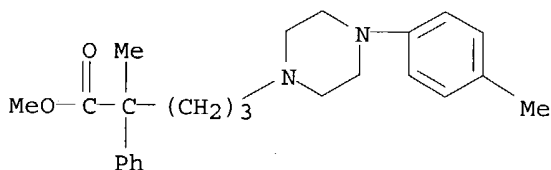
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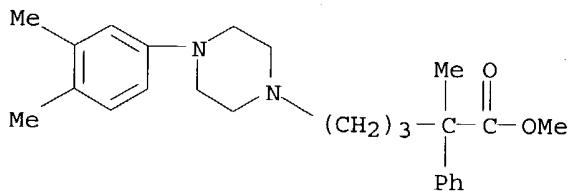
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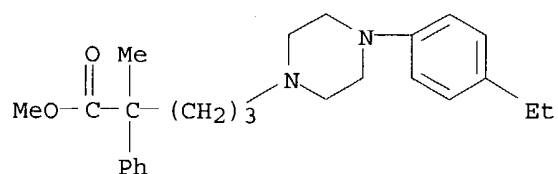
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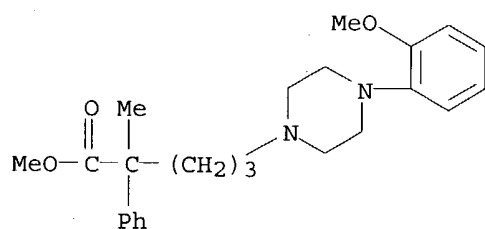
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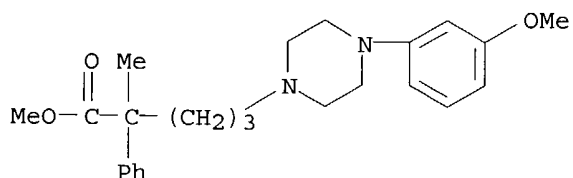
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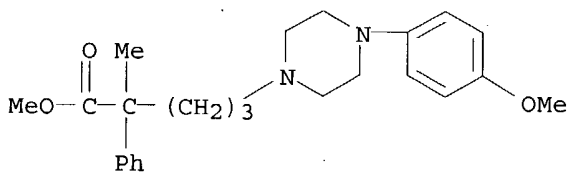
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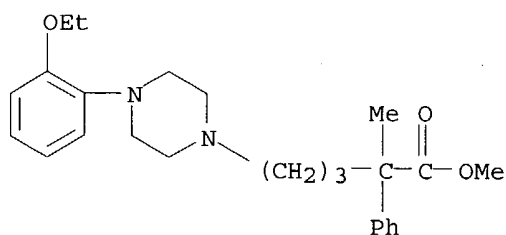
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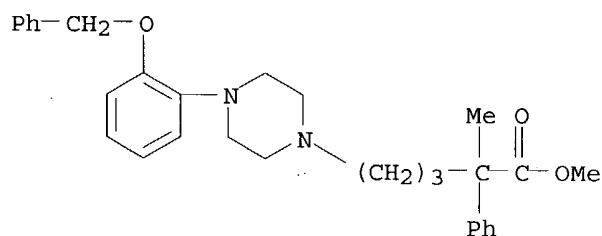
CN 1-Piperazinepentanoic acid, 4-(2-ethoxyphenyl)-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



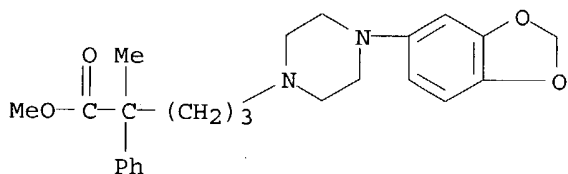
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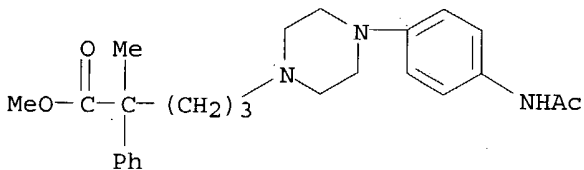
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RN 327030-27-3 CAPLUS

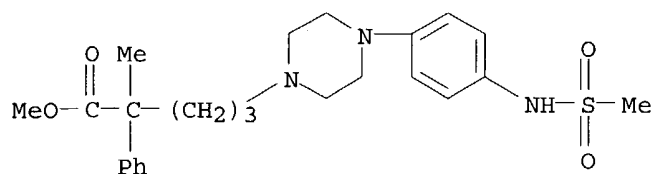
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RN 327030-28-4 CAPLUS

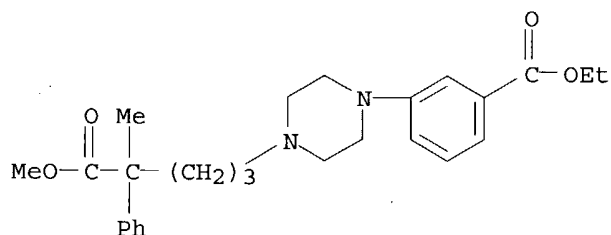
CN 1-Piperazinepentanoic acid, α -methyl-4-[4-[(methylsulfonyl)amino]phenyl]- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



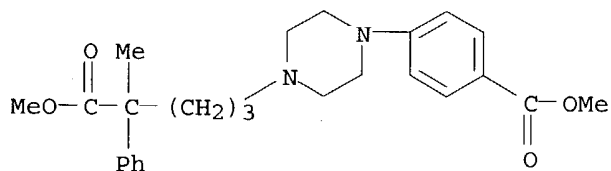
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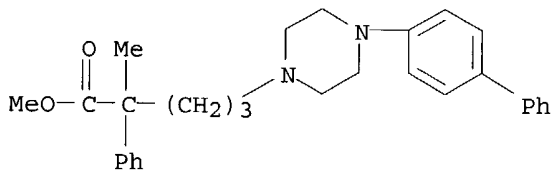
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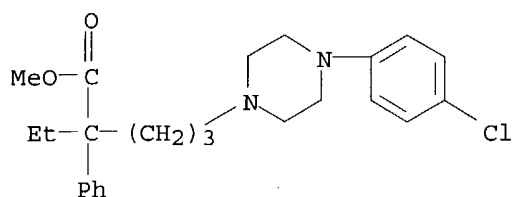
CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-4-yl-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-36-4 CAPLUS

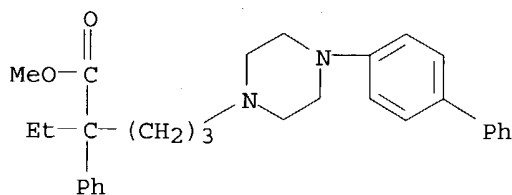
CN 1-Piperazinepentanoic acid, 4-(4-chlorophenyl)-α-ethyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



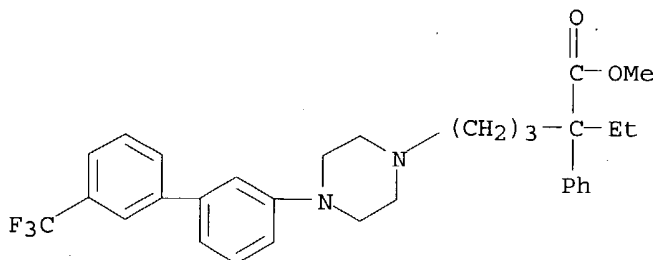
RN 327030-37-5 CAPLUS

CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-4-yl- α -ethyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



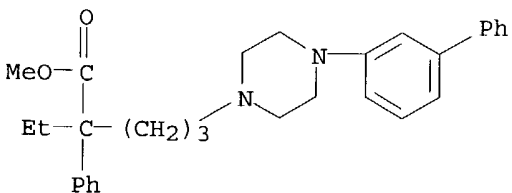
RN 327030-38-6 CAPLUS

CN 1-Piperazinepentanoic acid, α -ethyl- α -phenyl-4-[3'-(trifluoromethyl)[1,1'-biphenyl]-3-yl]-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-42-2 CAPLUS

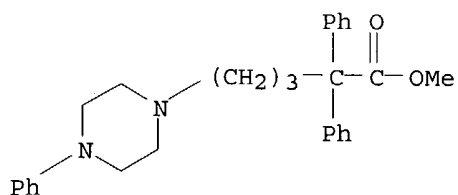
CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-3-yl- α -ethyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-43-3 CAPLUS

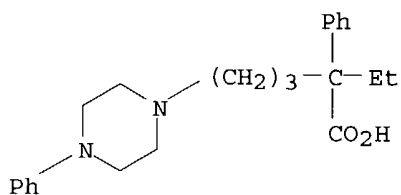
CN 1-Piperazinepentanoic acid, $\alpha,\alpha,4$ -triphenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



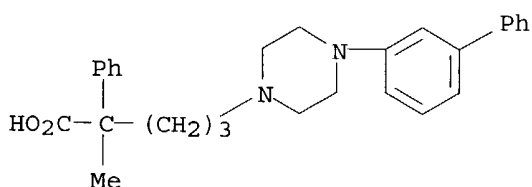
RN 327030-46-6 CAPLUS

CN 1-Piperazinepentanoic acid, α -ethyl- α ,4-diphenyl- (9CI) (CA INDEX NAME)



RN 327030-47-7 CAPLUS

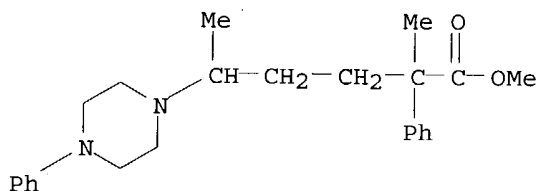
CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-3-yl- α -methyl- α -phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 327030-48-8 CAPLUS

CN 1-Piperazinepentanoic acid, α , δ -dimethyl- α ,4-diphenyl-, methyl ester (9CI) (CA INDEX NAME)

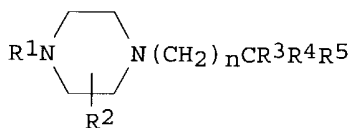


10/049795

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:136770 CAPLUS
DN 134:193434
TI Preparation of arylpiperazinylpentanecarboxylates and -hexanecarboxylates
as inhibitors of microsomal triglyceride transfer protein.
IN Lehmann-Lintz, Thorsten; Heckel, Armin; Thomas, Leo; Mark, Michael
PA Boehringer Ingelheim Pharma KG, Germany
SO Ger. Offen., 24 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

APPS

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19939516	A1	20010222	DE 1999-19939516	19990820
	WO 2001014355	A1	20010301	WO 2000-EP7976	20000816
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1210340	A1	20020605	EP 2000-962322	20000816
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
	JP 2003507463	T2	20030225	JP 2001-518443	20000816
PRAI	DE 1999-19939516	A	19990820		
	DE 1999-19939745	A	19990821		
	WO 2000-EP7976	W	20000816		
OS	MARPAT 134:193434				
GI					



I

AB Title compds. [I; n = 3, 4, 5; R1 = (substituted) Ph; R2 = H, alkyl; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, (substituted) Ph, naphthyl, heteroaryl; R4 = (substituted) Ph, naphthyl, heteroaryl; R5 = CO₂H, (substituted) alkoxy carbonyl, cycloalkoxy carbonyl], were prepared to reduce plasma levels of arterogenic lipoproteins (no data). Thus, 1-phenylpiperazine, Me 5-bromo-2-methyl-2-phenylpentanoate (preparation given), and Et₃N were stirred 42 h in MeOH to give 29.2% Me 2-methyl-2-phenyl-5-(4-phenylpiperazin-1-yl)pentanoate.

IT 327030-05-7P

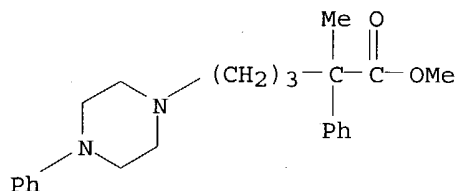
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylpiperazinylpentanecarboxylates and -hexanecarboxylates as inhibitors of microsomal triglyceride transfer protein)

RN 327030-05-7 CAPLUS

CN 1-Piperazinepentanoic acid, α -methyl- α ,4-diphenyl-, methyl

10/049795

ester (9CI) (CA INDEX NAME)



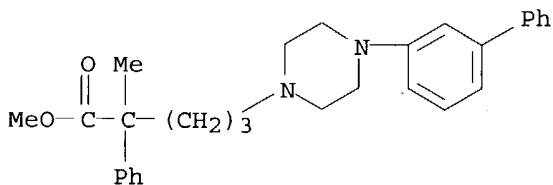
IT 327030-33-1P 327030-35-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of arylpiperazinylpentanecarboxylates as inhibitors of microsomal triglyceride transfer protein)

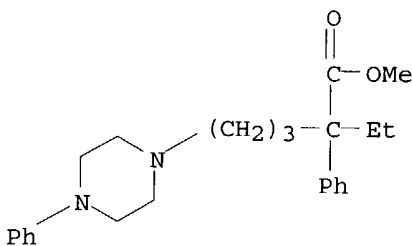
RN 327030-33-1 CAPLUS

CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-3-yl- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-35-3 CAPLUS

CN 1-Piperazinepentanoic acid, α -ethyl- α ,4-diphenyl-, methyl ester (9CI) (CA INDEX NAME)



IT 327030-08-0P 327030-09-1P 327030-10-4P
327030-11-5P 327030-12-6P 327030-13-7P
327030-14-8P 327030-15-9P 327030-16-0P
327030-17-1P 327030-18-2P 327030-19-3P
327030-20-6P 327030-21-7P 327030-22-8P
327030-23-9P 327030-24-0P 327030-25-1P
327030-26-2P 327030-27-3P 327030-28-4P
327030-29-5P 327030-30-8P 327030-31-9P
327030-36-4P 327030-37-5P 327030-38-6P
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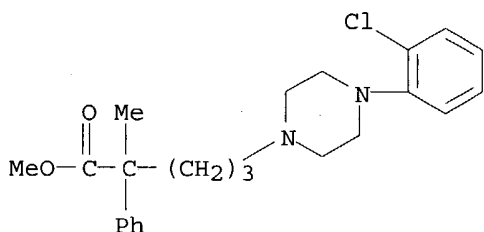
10/049795

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of arylpiperazinylpentanecarboxylates as inhibitors of microsomal triglyceride transfer protein)

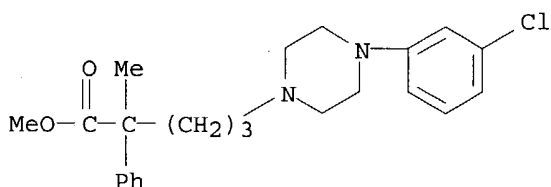
RN 327030-08-0 CAPLUS

CN 1-Piperazinepentanoic acid, 4-(2-chlorophenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



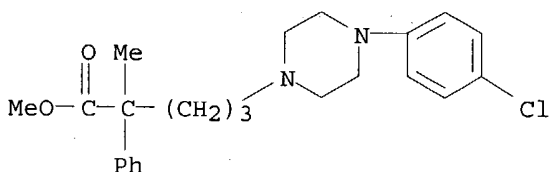
RN 327030-09-1 CAPLUS

CN 1-Piperazinepentanoic acid, 4-(3-chlorophenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



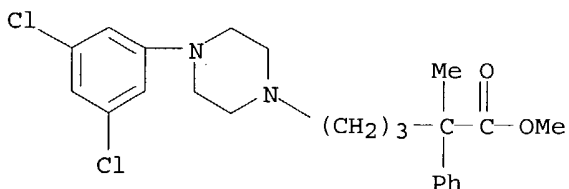
RN 327030-10-4 CAPLUS

CN 1-Piperazinepentanoic acid, 4-(4-chlorophenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-11-5 CAPLUS

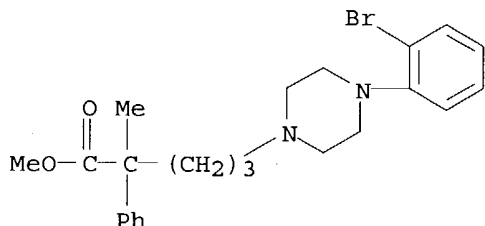
CN 1-Piperazinepentanoic acid, 4-(3,5-dichlorophenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



10/049795

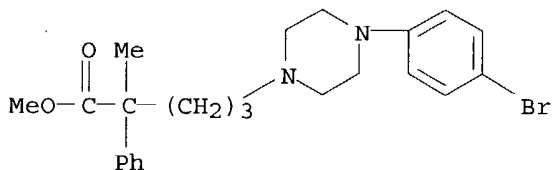
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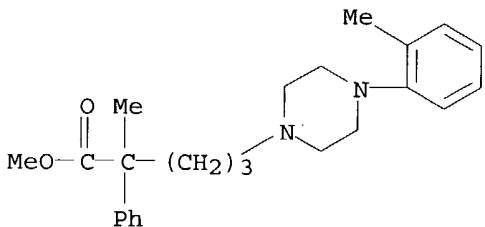
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CN 1-Piperazinepentanoic acid, 4-(4-bromophenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



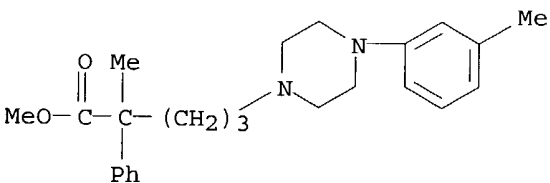
RN 327030-14-8 CAPLUS

CN 1-Piperazinepentanoic acid, α -methyl-4-(2-methylphenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-15-9 CAPLUS

CN 1-Piperazinepentanoic acid, α -methyl-4-(3-methylphenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)

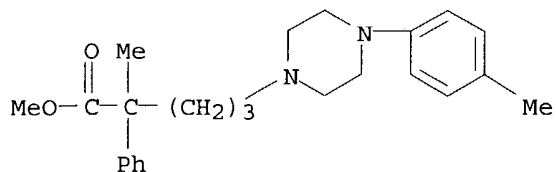


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CN 1-Piperazinepentanoic acid, α -methyl-4-(4-methylphenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)

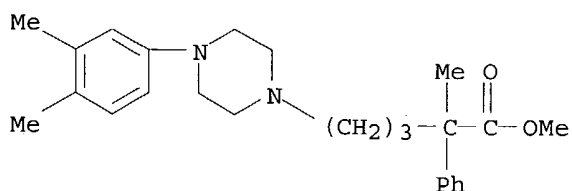
10/049795

phenyl-, methyl ester (9CI) (CA INDEX NAME)



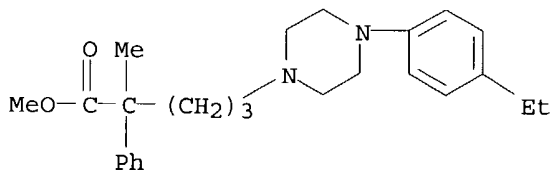
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CN 1-Piperazinepentanoic acid, 4-(3,4-dimethylphenyl)-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



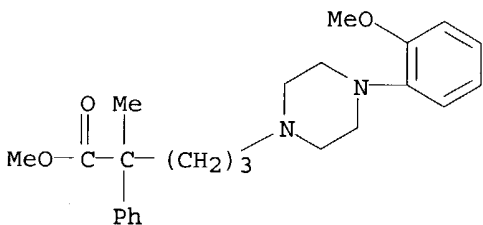
RN 327030-18-2 CAPLUS

CN 1-Piperazinepentanoic acid, 4-(4-ethylphenyl)-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-19-3 CAPLUS

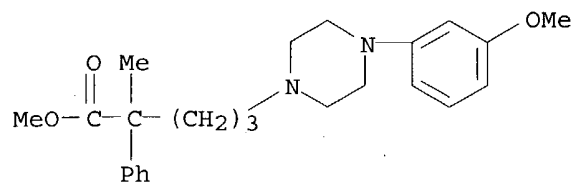
CN 1-Piperazinepentanoic acid, 4-(2-methoxyphenyl)-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



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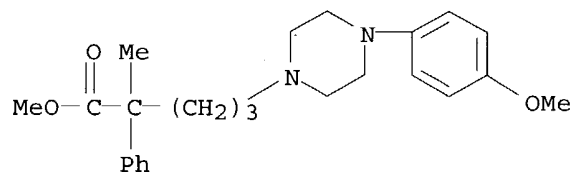
CN 1-Piperazinepentanoic acid, 4-(3-methoxyphenyl)-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



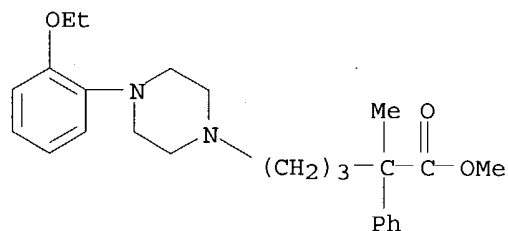
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CN 1-Piperazinepentanoic acid, 4-(4-methoxyphenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



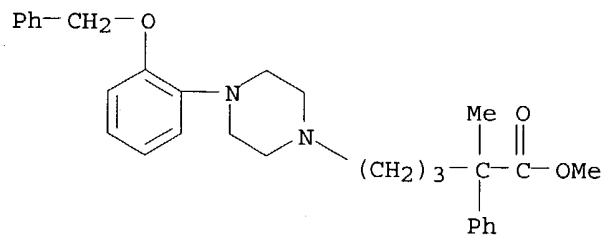
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CN 1-Piperazinepentanoic acid, 4-(2-ethoxyphenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-23-9 CAPLUS

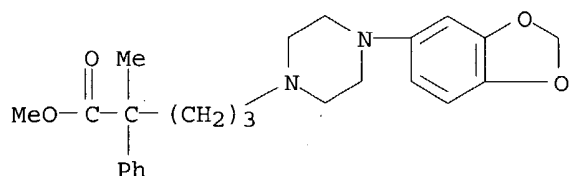
CN 1-Piperazinepentanoic acid, α -methyl- α -phenyl-4-[2-(phenylmethoxy)phenyl]-, methyl ester (9CI) (CA INDEX NAME)



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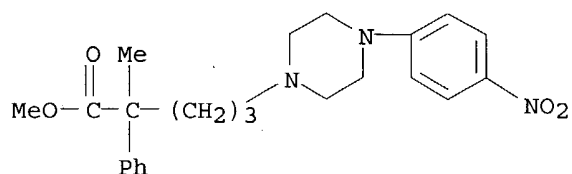
CN 1-Piperazinepentanoic acid, 4-(1,3-benzodioxol-5-yl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



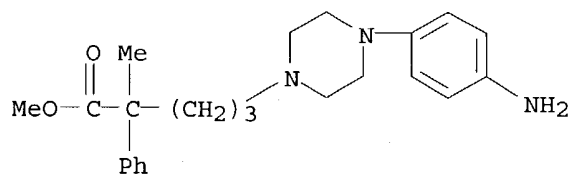
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CN 1-Piperazinepentanoic acid, α -methyl-4-(4-nitrophenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



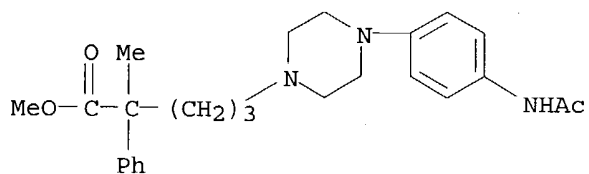
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CN 1-Piperazinepentanoic acid, 4-(4-aminophenyl)- α -methyl- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



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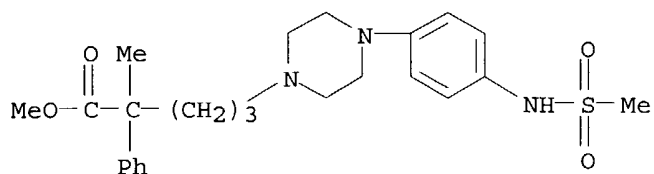
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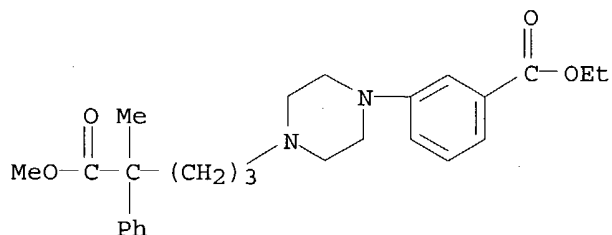
CN 1-Piperazinepentanoic acid, α -methyl-4-[4-[(methylsulfonyl)amino]phenyl]- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



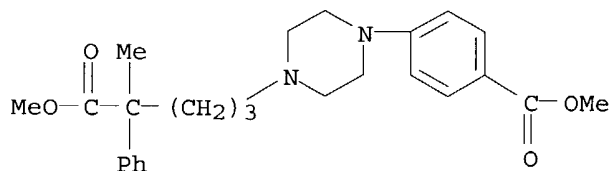
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CN 1-Piperazinepentanoic acid, 4-[3-(ethoxycarbonyl)phenyl]-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



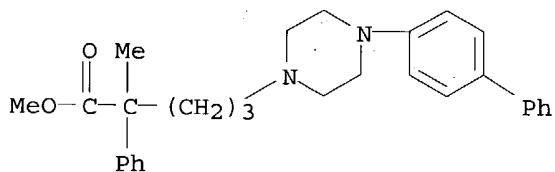
RN 327030-30-8 CAPLUS

CN 1-Piperazinepentanoic acid, 4-[4-(methoxycarbonyl)phenyl]-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-31-9 CAPLUS

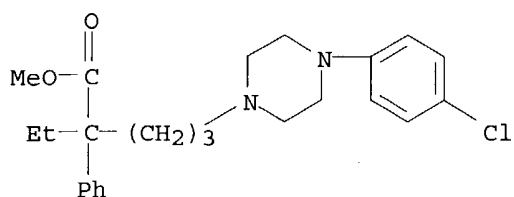
CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-4-yl-α-methyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-36-4 CAPLUS

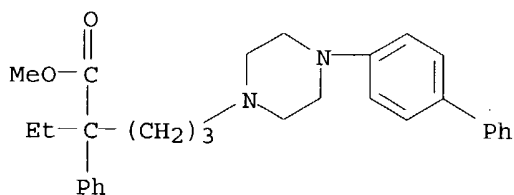
CN 1-Piperazinepentanoic acid, 4-(4-chlorophenyl)-α-ethyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



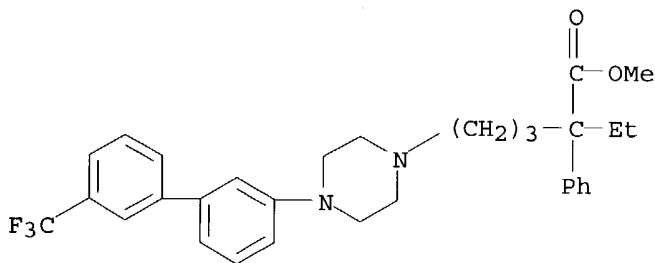
RN 327030-37-5 CAPLUS

CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-4-yl-α-ethyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



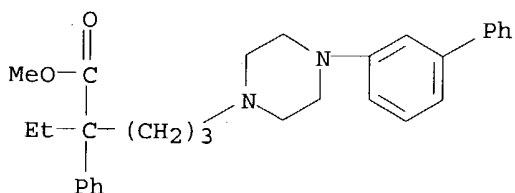
RN 327030-38-6 CAPLUS

CN 1-Piperazinepentanoic acid, α-ethyl-α-phenyl-4-[3'-(trifluoromethyl)[1,1'-biphenyl]-3-yl]-, methyl ester (9CI) (CA INDEX NAME)



RN 327030-42-2 CAPLUS

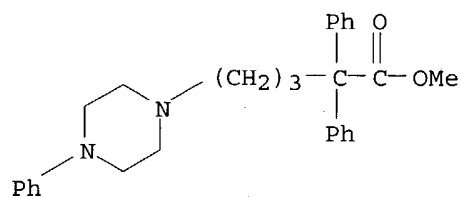
CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-3-yl-α-ethyl-α-phenyl-, methyl ester (9CI) (CA INDEX NAME)



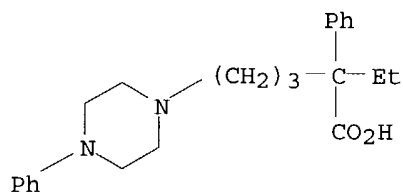
RN 327030-43-3 CAPLUS

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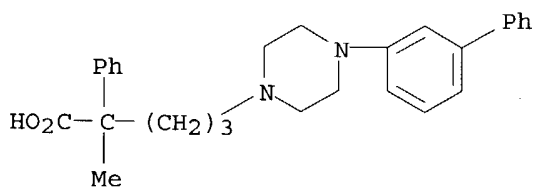
10/049795



RN 327030-46-6 CAPLUS
CN 1-Piperazinepentanoic acid, α -ethyl- α ,4-diphenyl- (9CI) (CA INDEX NAME)

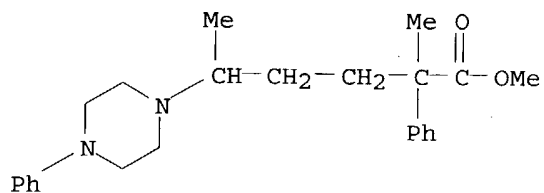


RN 327030-47-7 CAPLUS
CN 1-Piperazinepentanoic acid, 4-[1,1'-biphenyl]-3-yl- α -methyl- α -phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

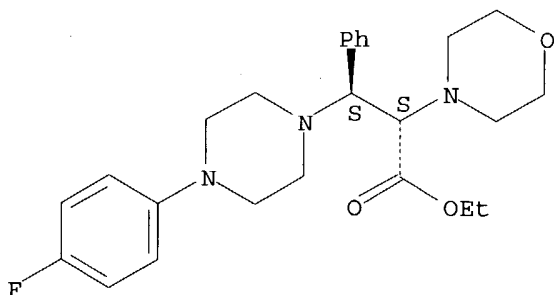
RN 327030-48-8 CAPLUS
CN 1-Piperazinepentanoic acid, α , δ -dimethyl- α ,4-diphenyl-, methyl ester (9CI) (CA INDEX NAME)



10/049795

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:758683 CAPLUS
DN 134:71128
TI Applications of Aziridinium Ions. Selective Syntheses of
 α,β -Diamino Esters, α -Sulfanyl- β -amino Esters,
 β -Lactams, and 1,5-Benzodiazepin-2-one
AU Chuang, Tsung-Hsun; Sharpless, K. Barry
CS Department of Chemistry and the Skaggs Institute for Chemical Biology, The
Scripps Research Institute, La Jolla, CA, 92037, USA
SO Organic Letters (2000), 2(23), 3555-3557
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
OS CASREACT 134:71128
AB A variety of nucleophiles, including amines, thiolates, and alkoxides,
were employed to open aziridinium ions. The latter are opened
stereospecifically and regioselectively at the C-3 position by a wide
range of amines, and thiolate nucleophiles attack predominately at the C-2
position. Poor regioselectivities (ca. 1:1) were observed using nucleophiles
derived from phenols, carboxylic acids, and imides. Base-mediated ring
closure of the aziridinium opening products, from primary amines, gave
 β -lactams and a 1,5-benzodiazepin-2-one in high yields.
IT 314277-96-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(ring cleavage of aziridinium ions via reactions with amines,
thiolates, and alkoxides)
RN 314277-96-8 CAPLUS
CN 4-Morpholineacetic acid, α -[(R)-[4-(4-fluorophenyl)-1-
piperazinyl]phenylmethyl]-, ethyl ester, (α R)-rel- (9CI) (CA INDEX
NAME)

Relative stereochemistry.

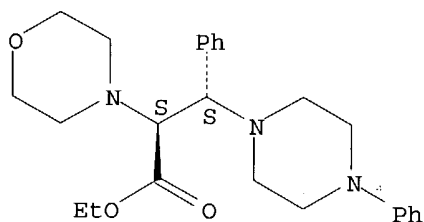


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/049795

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:634691 CAPLUS
DN 132:22730
TI Applications of Aziridinium Ions. Selective Syntheses of
 β -Aryl- α,β -diamino Esters
AU Chuang, Tsung-Hsun; Sharpless, K. Barry
CS Department of Chemistry and the Skaggs Institute for Chemical Biology, The
Scripps Research Institute, La Jolla, CA, 92037, USA
SO Organic Letters (1999), 1(9), 1435-1437
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
OS CASREACT 132:22730
AB α,β -Diamino esters are readily prepared through stereospecific
and regioselective opening of an aziridinium ion intermediate with a
variety of amines. The aziridinium ion is generated from the epoxide in
two steps.
IT 251967-14-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of β -aryl- α,β -diamino esters through
stereospecific and regioselective opening of an aziridinium ion
intermediate)
RN 251967-14-3 CAPLUS
CN 4-Morpholineacetic acid, α -[(R)-phenyl(4-phenyl-1-
piperazinyl)methyl]-, ethyl ester, (α R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/049795

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:128095 CAPLUS
DN 126:166501
TI N-Heterocycloalkyl carboxamides as serotonergic agents
IN Baudy, Reinhardt B.; Berta, Scott C.
PA American Home Products Corporation, USA
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5602128	A	19970211	US 1994-348651	19941202
PRAI	US 1994-348651		19941202		

OS MARPAT 126:166501

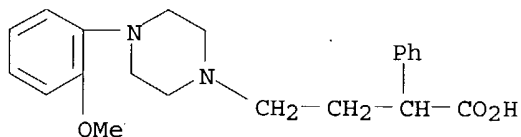
AB 4-[4-(2-Methoxyphenyl)piperazin-1-yl]-N-[(thio)morpholinyl]-2-phenylbutyramides and a pharmaceutically acceptable salt thereof, are useful as anxiolytic/antidepressant agents. Coupling of 4-[4-(2-methoxyphenyl)piperazin-1-yl]-2-phenylbutanoic acid with 4-(2-aminoethyl)morpholine in presence of triethylamine and N,N-bis(2-oxo-3-oxazolidinyl)phosphoramidic chloride gave 4-[4-(2-methoxyphenyl)piperazin-1-yl]-N-(2-morpholin-4-ylethyl)-2-phenylbutyramide (I). I displayed potent affinity for the serotonin 5-HT_{1A} receptor.

IT 156818-13-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(4-[4-(2-methoxyphenyl)piperazin-1-yl]-N-[(thio)morpholinyl]-2-phenylbutyramides as serotonergic agents)

RN 156818-13-2 CAPLUS

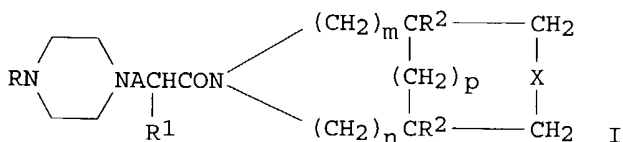
CN 1-Piperazinebutanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA INDEX NAME)



10/049795

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:446471 CAPLUS
 DN 125:114692
 TI Preparation of piperazine-containing bicyclic carboxamides as 5-HT1a
 receptor antagonists
 IN Cliffe, Ian Anthony; Mansell, Howard Langham; Ward, Terence James; Nelson,
 James Albert; Shah, Uresh Shantilal; Kanzelberger, Mira Ana
 PA John Wyeth and Brother Ltd., UK; American Home Products Corporation
 SO PCT Int. Appl., 29 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9609302	A1	19960328	WO 1995-GB2001	19950823
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TT, UA, UG, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5610154	A	19970311	US 1995-448962	19950524
	CA 2200443	AA	19960328	CA 1995-2200443	19950823
	AU 9533501	A1	19960409	AU 1995-33501	19950823
	AU 692917	B2	19980618		
	EP 782574	A1	19970709	EP 1995-929941	19950823
	EP 782574	B1	20020327		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1158615	A	19970903	CN 1995-195207	19950823
	CN 1043764	B	19990623		
	BR 9508979	A	19971028	BR 1995-8979	19950823
	JP 10505853	T2	19980609	JP 1995-510658	19950823
	HU 77940	A2	19981228	HU 1998-408	19950823
	AT 215083	E	20020415	AT 1995-929941	19950823
	ES 2170802	T3	20020816	ES 1995-929941	19950823
	PT 782574	T	20020830	PT 1995-95929941	19950823
	IL 115085	A1	19990620	IL 1995-115085	19950828
	ZA 9507449	A	19970305	ZA 1995-7449	19950905
	TW 424092	B	20010301	TW 1995-84109809	19950919
	FI 9701177	A	19970520	FI 1997-1177	19970320
PRAI	GB 1994-19024	A	19940921		
	WO 1995-GB2001	W	19950823		
OS	MARPAT 125:114692				
GI					



AB The title compds. [I; A = (un)substituted C1-2 alkylene; R = mono or bicyclic aryl or heteroaryl; R1 = aryl, arylalkyl; X = CR2:CR2, (CR2)q; R2 = H, lower alkyl; m, n = 0-2; p, q = 0-3], which are 5-HT1a receptor

10/049795

antagonists, useful as anxiolytics (no data), are prepared Thus, 4-[4-(2-methoxyphenyl)piperazin-1-yl]-2-phenylbutanoic acid was condensed with desmethyldropane and the resultant free base salified with aqueous HCl, producing 1-(8-azabicyclo[3.2.1]oct-8-yl)-4-[4-(2-methoxyphenyl)piperazin-1-yl]-2-phenylbutan-1-one hydrochloride hemihydrate, m.p. 225-228° (decomposition), which demonstrated a IC50 of 3.3 nM in a rat hippocampal membrane homogenate-derived 5-HT1a receptor-binding assay.

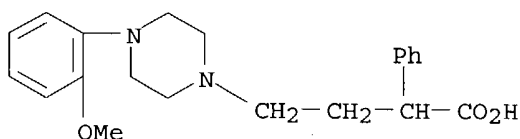
IT 156818-13-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of piperazine-containing bicyclic carboxamides as 5-HT1a receptor antagonists)

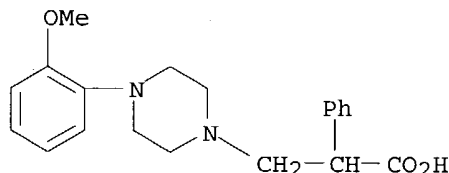
RN 156818-13-2 CAPLUS

CN 1-Piperazinebutanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA INDEX NAME)



10/049795

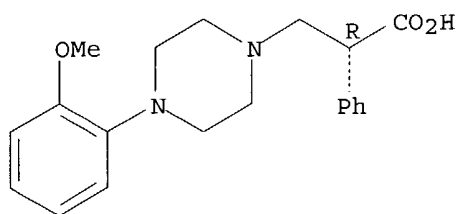
L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:123207 CAPLUS
DN 124:249645
TI Structure-activity relationship studies of CNS agents. Part 24. New analogs of N-tert.-butyl-3-[4-(2-methoxyphenyl)-1-piperazinyl]-2-phenylpropanamide
AU Boksa, J.; Klodzinska, Aleksandra; Charakchieva-Minol, Sijka; Chojnacka-Wojcik, Ewa; Mokrosz, J. L.
CS Inst. Pharmacology, Polish Acad. Sci., Krakow, Pol.
SO Pharmazie (1996), 51(2), 72-6
CODEN: PHARAT; ISSN: 0031-7144
PB Govi-Verlag Pharmazeutischer Verlag
DT Journal
LA English
AB A series of new N-substituted derivs. of 3-[4-(2-methoxyphenyl)-1-piperazinyl]-2-phenylpropanamide were synthesized and their 5-HT_{1A}, 5-HT_{2A}, and α_1 receptor affinities were determined All the compds. were highly potent 5-HT_{1A} ligands with a moderate or low 5-HT_{2A} and α_1 affinity. The 5-HT_{2A} affinity of these compds. depended on the volume of amide substituents. None of the investigated racemic mixts. antagonized the 8-OH-DPAT-induced lower lip retraction in rats.
IT **129394-10-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure-5-HT receptor agonist activity relations of arylpiperazine derivs.)
RN 129394-10-1 CAPLUS
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA INDEX NAME)



IT **175274-25-6P 175274-26-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-5-HT receptor agonist activity relations of arylpiperazines)
RN 175274-25-6 CAPLUS
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/049795

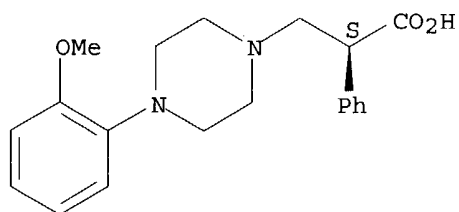


● 2 HCl

RN 175274-26-7 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-,
dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

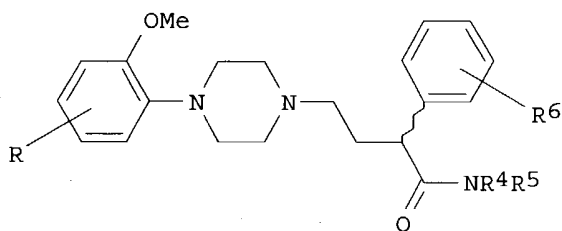


● 2 HCl

10/049795

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:947094 CAPLUS
DN 124:146200
TI 4-[4-(2-Methoxyphenyl)piperazin-1-yl]-2-phenyl-N-alkynylbutyramides as
serotonergic agents
IN Baudy, Reinhardt B.; Berta, Scott C.
PA American Home Products Corp., USA
SO U.S., 5 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5451584	A	19950919	US 1994-337810	19941110
PRAI	US 1994-337810		19941110		
OS	MARPAT 124:146200				
GI					



AB Carboxamides I where: R and R6 are members independently selected from the group consisting of H, CN, OR2, NO2, NR2R3, NR2COR3, NR2COOR3, COR2, COOR2, CONR2R3, SR2, SOR2, SO2R2, SO2NR2R3, alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms, perhaloalkyl of 1 to 6 carbon atoms, and a halogen; in which R2 and R3 are alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, alkynyl of 2 to 6 carbon atoms, Ph, or benzyl; R4 is a member selected from the group consisting of H, alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms and alkynyl of 2 to 6 carbon atoms; R5 is alkynyl of 2 to 8 carbon atoms or 1-alkynylcycloalkyl in which the alkynyl group has 2 to 6 carbon atoms and the cycloalkyl group has 3 to 10 carbon atoms; or a pharmaceutically acceptable salt thereof, are useful anxiolytic/antidepressant agents. Thus, e.g., coupling of 4-[4-(2-methoxyphenyl)piperazin-1-yl]-2-phenylbutanoic acid with propargylamine in presence of triethylamine and N,N-bis(2-oxo-3-oxazolidinyl)phosphoramidic chloride, followed by treatment with ethanolic HCl afforded 4-[4-(2-methoxyphenyl)piperazin-1-yl]-2-phenyl-N-prop-2-ynylbutyramide dihydrochloride (I.2HCl; R = R6 = H, NR4R5 = propargylamino) which displayed high affinity for the serotonin 5-HT1A receptor subtype, with IC50 = 44.9 nM.

IT 156818-13-2

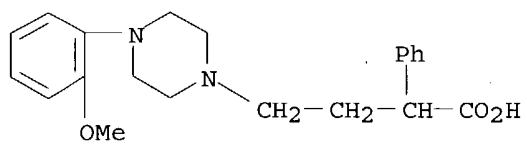
RL: RCT (Reactant); RACT (Reactant or reagent)

(4-[4-(2-methoxyphenyl)piperazin-1-yl]-2-phenyl-N-alkynylbutyramides as serotonergic agents useful as anxiolytics/antidepressants)

RN 156818-13-2 CAPLUS

CN 1-Piperazinebutanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA INDEX NAME)

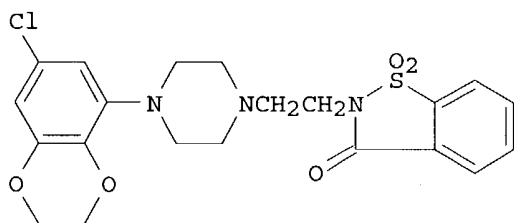
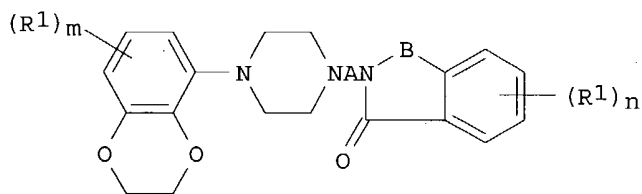
10/049795



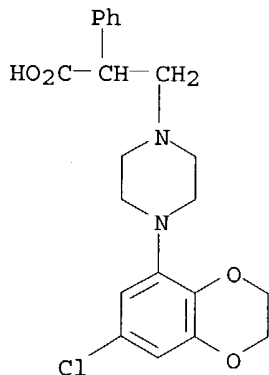
10/049795

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:422806 CAPLUS
DN 122:187611
TI Preparation of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivatives
having 5-HT1a-antagonistic activity.
IN Hartog, Jan; Van Steen, B. J.; Mos, Johannes; Schipper, Jacques
PA Duphar International Research B.V., Neth.
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 633260	A1	19950111	EP 1994-201900	19940701
	EP 633260	B1	20011107		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2127084	AA	19950106	CA 1994-2127084	19940629
	FI 9403149	A	19950106	FI 1994-3149	19940630
	NO 9402471	A	19950106	NO 1994-2471	19940630
	JP 07215972	A2	19950815	JP 1994-170370	19940630
	US 5462942	A	19951031	US 1994-269086	19940630
	HU 75155	A2	19970428	HU 1994-1965	19940630
	HU 218215	B	20000628		
	CZ 286503	B6	20000412	CZ 1994-1597	19940630
	SK 281681	B6	20010611	SK 1994-788	19940630
	ZA 9404787	A	19950220	ZA 1994-4787	19940701
	CN 1106813	A	19950816	CN 1994-115999	19940701
	CN 1044244	B	19990721		
	AT 208385	E	20011115	AT 1994-201900	19940701
	PT 633260	T	20020429	PT 1994-94201900	19940701
	ES 2167346	T3	20020516	ES 1994-201900	19940701
	AU 9466139	A1	19950112	AU 1994-66139	19940704
	AU 680900	B2	19970814		
	RU 2118322	C1	19980827	RU 1994-23250	19940704
	IL 110209	A1	20000229	IL 1994-110209	19940704
PRAI	EP 1993-201950	A	19930705		
OS	CASREACT 122:187611; MARPAT 122:187611				
GI					



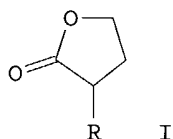
- AB Title compds. (I; R1 = halo, lower alkyl, alkoxy, OH, CF₃, cyano; m = 1,2; n = 0,1; A = C2-6 alkylene which may be substituted with ≥1 lower alkyl groups or a monocyclic (hetero)aryl group; B = CH₂, CH₂CH₂, CO, S, SO, SO₂), were prepared. Thus, saccharin was heated with 1-(7-chloro-2,3-dihydro-1,4-benzodioxin-5-yl)-4-(2-chloroethyl)piperazine and NaH in DMF to give title compound (II). In general I were selective for 5-HT_{1A} receptors, antagonize the effects of 8-OH-DPAT in rats, and have good oral bioavailability.
- IT **161612-51-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivs. having 5-HT_{1A}-antagonistic activity)
- RN 161612-51-7 CAPLUS
- CN 1-Piperazinepropanoic acid, 4-(7-chloro-2,3-dihydro-1,4-benzodioxin-5-yl)-α-phenyl- (9CI) (CA INDEX NAME)



10/049795

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:533946 CAPLUS
DN 121:133946
TI Preparation of α -aryl- γ -butyrolactones
IN Shepherd, Robin Gerald
PA John Wyeth and Brother Ltd., UK
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9412487	A1	19940609	WO 1993-GB2427	19931125
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2150948	AA	19940609	CA 1993-2150948	19931125
	AU 9455324	A1	19940622	AU 1994-55324	19931125
	EP 672039	A1	19950920	EP 1994-900256	19931125
	EP 672039	B1	19970709		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 08503939	T2	19960430	JP 1994-512915	19931125
	JP 3274866	B2	20020415		
	AT 155134	E	19970715	AT 1994-900256	19931125
	ES 2105597	T3	19971016	ES 1994-900256	19931125
	ZA 9308873	A	19950526	ZA 1993-8873	19931126
	US 5629432	A	19970513	US 1995-436186	19950516
PRAI	GB 1992-25257	A	19921203		
	WO 1993-GB2427	W	19931125		
OS	CASREACT 121:133946; MARPAT 121:133946				
GI					



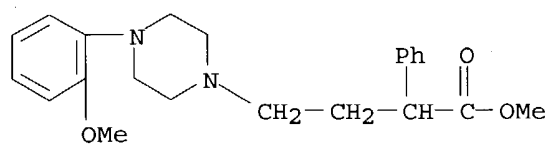
AB Title compds. [I; R = (un)substituted Ph, or (bicyclic)heteroaryl] were prepared by condensation of $\text{RCH}(\text{CO}_2\text{R}_1)\text{CO}_2\text{R}_2$ (R_1, R_2 = alkyl) with $\text{YCH}_2\text{CH}_2\text{OZ}$ (Y = leaving group; Z = protecting group) to give $\text{RC}(\text{CO}_2\text{R}_1)(\text{CO}_2\text{R}_2)\text{CH}_2\text{CH}_2\text{OZ}$ followed by hydrolysis. The lactones are of use as intermediates for preparing 5-HT_{1A} binding agents (sic). Thus, $\text{PhCH}(\text{CO}_2\text{Et})_2$ was condensed with $\text{BrCH}_2\text{CH}_2\text{OAc}$ to give $\text{PhC}(\text{CO}_2\text{Et})_2\text{CH}_2\text{CH}_2\text{OAc}$ which was refluxed 2h with NaOH in aqueous MeOH to give 89% (this step) I (R = Ph). The latter was converted in 6 steps to (-)-2,3,4,5,6,7-hexahydro-1-[4-[4-(2-methoxyphenyl)piperazino]-2-phenylbutyryl]-1H-azepine hydrochloride.

IT **141733-63-3P 156818-13-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of drug)

RN 141733-63-3 CAPLUS

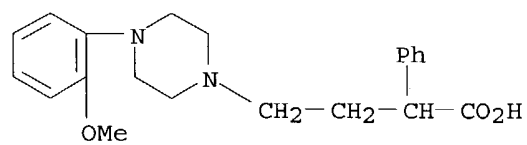
CN 1-Piperazinebutanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



RN 156818-13-2 CAPLUS

CN 1-Piperazinebutanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA
INDEX NAME)



10/049795

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:491799 CAPLUS
DN 121:91799
TI Pharmaceutical piperazine derivatives
IN Cliffe, Ian Anthony; Ifill, Anderson Decourtney; White, Alan Chapman
PA John Wyeth and Brother Ltd., UK
SO Brit. UK Pat. Appl., 12 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2271930	A1	19940504	GB 1993-21690	19931021
	GB 2271930	B2	19960724		
PRAI	GB 1992-23014		19921103		

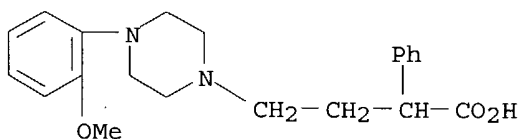
AB 4-[4-(2-Methoxyphenyl)piperazin-1-yl]-2-phenylbutanoic acid and the pharmaceutically acceptable salts thereof are useful as 5-HT_{1A}-antagonists. The compds. act primarily at peripheral 5-HT_{1A} sites and can be used in treating gastrointestinal disorders in humans and other mammals.

IT **156818-13-2P**

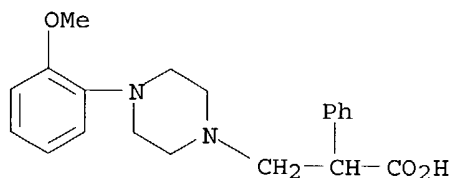
RL: PREP (Preparation)
(preparation of, as 5-HT_{1A} antagonist)

RN 156818-13-2 CAPLUS

CN 1-Piperazinebutanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA INDEX NAME)



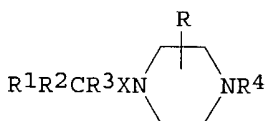
L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:485794 CAPLUS
DN 119:85794
TI (S)-N-tert-Butyl-3-(4-(2-methoxyphenyl)piperazin-1-yl)-2-phenylpropanamide
[(S)-WAY-100135]: a selective antagonist at presynaptic and postsynaptic
5-HT_{1A} receptors
AU Cliffe, Ian A.; Brightwell, Christopher I.; Fletcher, Allan; Forster,
Elaine A.; Mansell, Howard L.; Reilly, Yvonne; Routledge, Carol; White,
Alan C.
CS Dep. Med. Chem., Wyeth Res. (UK), Taplow/Berkshire, SL6 0PH, UK
SO Journal of Medicinal Chemistry (1993), 36(10), 1509-10
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB The synthesis and pharmacol. properties of S-(+)-WAY-100135 are reported.
The compound was a highly selective and potent antagonist at presynaptic and
postsynaptic 5-HT_{1A} receptors. The binding affinity at 5-HT_{1A} sites was
15.5 nM and the affinity at other 5-HT, noradrenergic, and dopaminergic D₂
sites was >1000 nM. In rats, (S)-WAY-100135 did not produce 5-HT_{1A}
agonist-like behaviors (up to 10 mg/kg i.v.) but blocked the effects of
8-OH-DPAT. Microdialysis expts. showed that (S)-WAY-100135 at 10 mg/kg
s.c. was without a significant effect on extracellular levels of 5-HT in
the rat brain hippocampus and completely blocked the effects of 8-OH-DPAT.
IT **129394-10-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, with butylamine)
RN 129394-10-1 CAPLUS
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA
INDEX NAME)



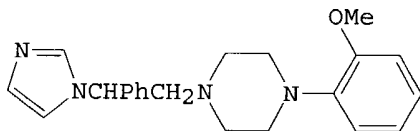
10/049795

L4 ANSWER 14 OF 21 CAPLUS. COPYRIGHT 2004 ACS on STN
AN 1992:490321 CAPLUS
DN 117:90321
TI Piperazine derivatives
IN Ward, Terence James; Warrellow, Graham John
PA John Wyeth and Brother Ltd., UK
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 479546	A2	19920408	EP 1991-308969	19911001
	EP 479546	A3	19920603		
	EP 479546	B1	19961030		
	R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE				
	AU 9184883	A1	19920409	AU 1991-84883	19910930
	AU 642532	B2	19931021		
	US 5177078	A	19930105	US 1991-768147	19910930
	GB 2248616	A1	19920415	GB 1991-20856	19911001
	GB 2248616	B2	19940615		
	JP 04257570	A2	19920911	JP 1991-253585	19911001
	AT 144772	E	19961115	AT 1991-308969	19911001
	ES 2094204	T3	19970116	ES 1991-308969	19911001
	CA 2052619	AA	19920404	CA 1991-2052619	19911002
	HU 59394	A2	19920528	HU 1991-3160	19911003
	HU 217813	B	20000428		
	IL 101166	A1	20000813	IL 1992-101166	19920306
PRAI	GB 1990-21453	A	19901003		
OS	MARPAT 117:90321				
GI					



I



II

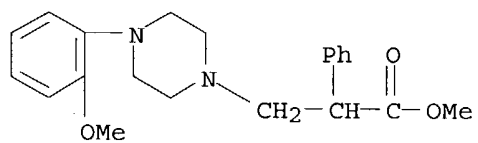
AB Piperazines I (X = alkylene; R = H, alkyl; R₁, R₄ = aryl, heteroaryl; R₂ = mono- or bicyclic heterocyclic; R₃ = H, OH, alkyl) were prepared. Thus, 1-(2-methoxyphenyl)piperazine was treated with styrene oxide followed by imidazole to give the piperazine II. II had 5-hydroxytryptamine type 1A receptor antagonist activity in rats at a min. ED of 1 mg/kg s.c. and 10 mg/kg orally.

IT 132708-57-7 141733-63-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with acetamidoxime)

RN 132708-57-7 CAPLUS

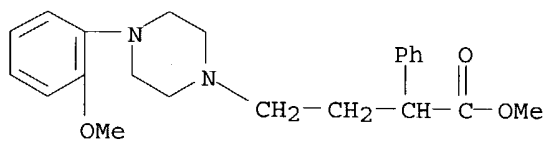
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)

10/049795



RN 141733-63-3 CAPLUS

CN 1-Piperazinebutanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



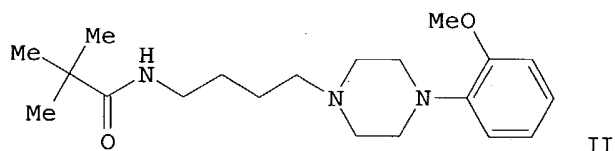
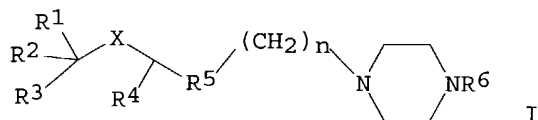
10/049795

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:164279 CAPLUS
DN 114:164279
TI Preparation of 1-aryl-4-carboxyalkylpiperazines and related compounds as
5HT1A antagonists
IN Cliffe, Ian Anthony; Abou-Gharbia, Magid Abdel Megid; Yardley, John
Patrick
PA American Home Products Corp., USA; John Wyeth and Brother Ltd.
SO Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 395313	A2	19901031	EP 1990-304251	19900420
	EP 395313	A3	19910508		
	EP 395313	B1	19991215		
	R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE				
	US 4988814	A	19910129	US 1989-428148	19891027
	CA 2015033	AA	19901022	CA 1990-2015033	19900420
	CA 2015033	C	20000606		
	AU 9053778	A1	19901025	AU 1990-53778	19900420
	AU 619677	B2	19920130		
	GB 2230780	A1	19901031	GB 1990-8924	19900420
	GB 2230780	B2	19921021		
	HU 54667	A2	19910328	HU 1990-2503	19900420
	DD 296921	A5	19911219	DD 1990-339954	19900420
	ZA 9003019	A	19911224	ZA 1990-3019	19900420
	ZA 9003020	A	19911224	ZA 1990-3020	19900420
	DD 297968	A5	19920130	DD 1990-339955	19900420
	FI 93832	B	19950228	FI 1990-1982	19900420
	FI 93832	C	19950612		
	KR 142417	B1	19980601	KR 1990-5531	19900420
	EP 955296	A2	19991110	EP 1999-108070	19900420
	EP 955296	A3	20000119		
	R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE				
	AT 187718	E	20000115	AT 1990-304251	19900420
	ES 2140374	T3	20000301	ES 1990-304251	19900420
	JP 03020263	A2	19910129	JP 1990-106300	19900421
	JP 3054677	B2	20000619		
	IL 94160	A1	19940624	IL 1990-94160	19900422
	US 5364849	A	19941115	US 1992-911996	19920710
	GB 2255976	A1	19921125	GB 1992-15425	19920720
	GB 2255976	B2	19921125		
	US 5382583	A	19950117	US 1992-998887	19921229
	US 5340812	A	19940823	US 1993-1428	19930107
	US 5420278	A	19950530	US 1994-248124	19940524
	US 5541326	A	19960730	US 1994-339000	19941114
	GR 3032634	T3	20000531	GR 2000-400332	20000210
PRAI	GB 1989-9209	A	19890422		
	US 1989-428148	A	19891027		
	GB 1989-24323	A	19891028		
	US 1990-511150	B2	19900419		
	EP 1990-304251	A3	19900420		
	GB 1990-8925	A3	19900420		
	US 1991-748496	B1	19910822		
	US 1991-748497	B1	19910822		
	US 1991-756932	B1	19910909		
	US 1992-911996	A3	19920710		

10/049795

US 1992-998887 A3 19921229
OS CASREACT 114:164279; MARPAT 114:164279
GI



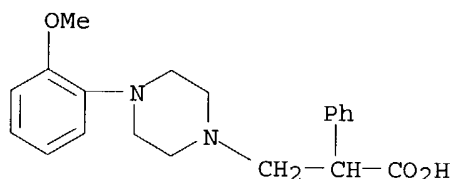
AB The title compds. [I; R1 = alkyl; R2, R3 = alkyl; R2R3 = cycloalkyl, 5-norbornen-2-yl; X = CO2, OCO2, NR7CO, NHNHCO, ONR7CO, CONR7, etc.; R4 = H, alkyl; R5 = R4, hydroxyalkyl, (substituted) Ph, PhCH2; R6 = (substituted) Ph, PhCH2, pyridinyl, pyrimidinyl, pyrazinyl; R7 = H, alkyl (substituted) Ph, PhCH2; n = 1-5], were prepared Thus, 4-(2-methoxyphenyl)-1-piperazinebutanamine, Et3N, and Me3CCOCl were stirred overnight in CH2Cl2 to give 38% title compound II which at 0.1 μ M gave 100% displacement of 3H-dipropylaminotetralin from 5-HT1A receptors.

IT **129394-10-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of, in preparation of 5-HT1A antagonist)

RN 129394-10-1 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA INDEX NAME)

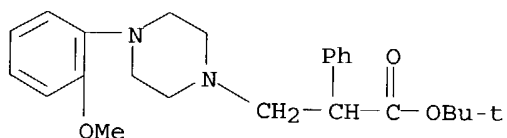


IT **133025-21-5P 133025-22-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT1A antagonist)

RN 133025-21-5 CAPLUS

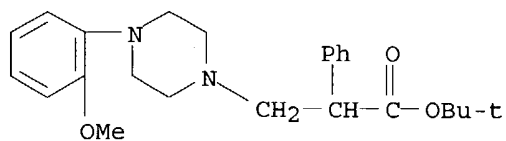
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 133025-22-6 CAPLUS

10/049795

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-,
1,1-dimethylethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

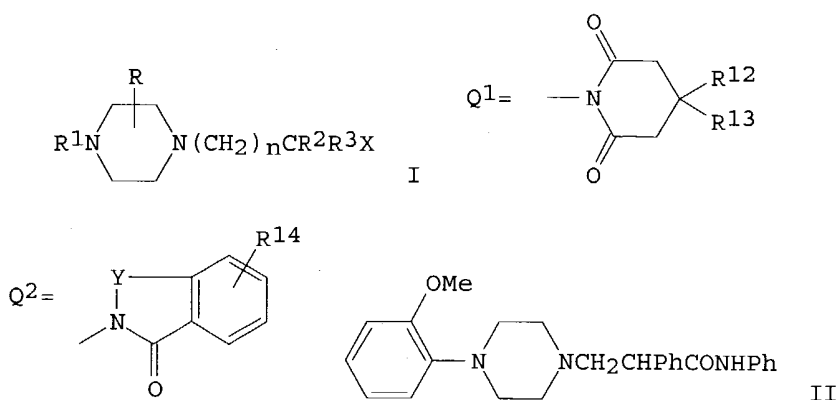


●2 HCl

10/049795

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:143444 CAPLUS
DN 114:143444
TI Preparation of 1-aryl-4-carboxyalkylpiperazines and related compounds as
serotonergic antagonists
IN Cliffe, Ian Anthony
PA John Wyeth and Brother Ltd., UK
SO Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 395312	A2	19901031	EP 1990-304250	19900420
	EP 395312	A3	19910508		
	EP 395312	B1	19990512		
	R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE				
	CA 2015034	AA	19901022	CA 1990-2015034	19900420
	CA 2015034	C	20000801		
	AU 9053779	A1	19901025	AU 1990-53779	19900420
	AU 619678	B2	19920130		
	GB 2230781	A1	19901031	GB 1990-8925	19900420
	GB 2230781	B2	19930428		
	HU 54666	A2	19910328	HU 1990-2504	19900420
	DD 296921	A5	19911219	DD 1990-339954	19900420
	ZA 9003019	A	19911224	ZA 1990-3019	19900420
	ZA 9003020	A	19911224	ZA 1990-3020	19900420
	DD 297968	A5	19920130	DD 1990-339955	19900420
	IL 94151	A1	19950831	IL 1990-94151	19900420
	AT 179973	E	19990515	AT 1990-304250	19900420
	ES 2130116	T3	19990701	ES 1990-304250	19900420
	JP 03011059	A2	19910118	JP 1990-106299	19900421
	JP 3036786	B2	20000424		
	US 5364849	A	19941115	US 1992-911996	19920710
	GB 2255976	A1	19921125	GB 1992-15425	19920720
	GB 2255976	B2	19921125		
	US 5382583	A	19950117	US 1992-998887	19921229
	US 5340812	A	19940823	US 1993-1428	19930107
	US 5420278	A	19950530	US 1994-248124	19940524
	US 5541326	A	19960730	US 1994-339000	19941114
PRAI	GB 1989-9209	A	19890422		
	GB 1989-24323	A	19891028		
	US 1990-511150	B2	19900419		
	GB 1990-8925	A3	19900420		
	US 1991-748496	B1	19910822		
	US 1991-748497	B1	19910822		
	US 1991-756932	B1	19910909		
	US 1992-911996	A3	19920710		
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OS	MARPAT 114:143444				
GI					



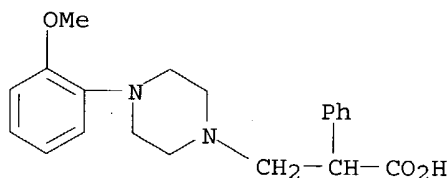
AB The title compds. [I; R = H, alkyl; R₁ = aryl, N-containing heteroaryl; R₂ = H, alkyl; R₃ = aryl, alkyl, arylalkyl; X = O₂CR₁₀, CO₂R₆, CONR₅R₉, OCO₂R₆, NR₄COR₆, Q₁, Q₂, etc.; R₄ = H, alkyl; R₆ = alkyl, cycloalkyl, arylalkyl; R₉ = H, alkyl, cycloalkyl, aryl, arylalkyl, 8-azaspiro[4.5]deca-7,9-dione-8-yl-alkyl, etc.; R₁₂, R₁₃ = alkyl; R₁₂R₁₃C = cycloalkyl; R₁₄ = H, halo, alkyl, alkoxy; Y = CO, SO₂; n = 1, 2] were prepared. Thus, 1-(2-methoxyphenyl)piperazine was refluxed 18 h with atropic acid in EtOH to give α-[1-[4-(2-methoxyphenyl)piperazinyl]methyl]benzeneacetic acid. The latter in CH₂Cl₂ was treated with carbonyldiimidazole and then aniline to give title compound II. I bound to rat hippocampal 5-HT_{1A} receptors with IC₅₀'s of 8-127 nM.

IT 129394-10-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification or amidation of)

RN 129394-10-1 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)-α-phenyl- (9CI) (CA INDEX NAME)

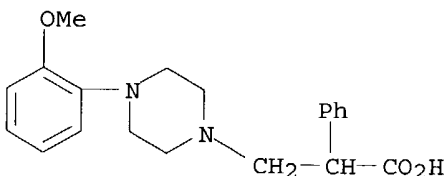


IT 129394-10-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for serotonergic antagonist)

RN 129394-10-1 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)-α-phenyl- (9CI) (CA INDEX NAME)

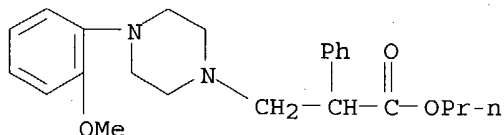


IT 132708-27-1P 132708-44-2P 132708-45-3P
 132708-57-7P 132708-68-0P 132708-89-5P
 132708-90-8P 132709-05-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as serotonergic antagonist)

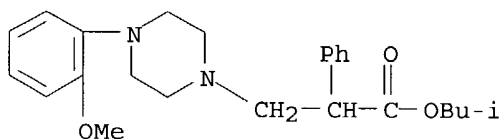
RN 132708-27-1 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, propyl ester (9CI) (CA INDEX NAME)



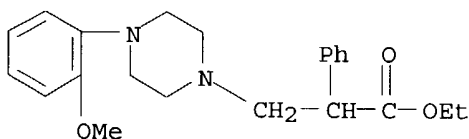
RN 132708-44-2 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



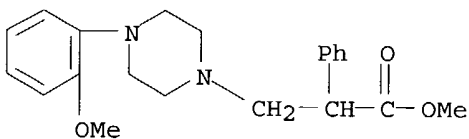
RN 132708-45-3 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 132708-57-7 CAPLUS

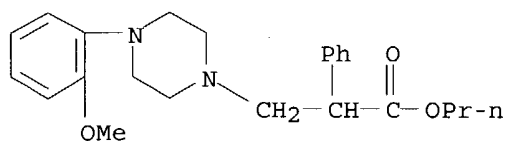
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 132708-68-0 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, propyl ester, dihydrochloride (9CI) (CA INDEX NAME)

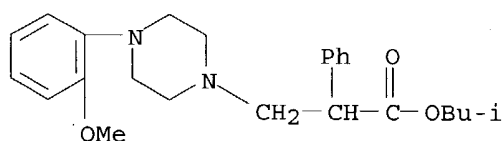
10/049795



●2 HCl

RN 132708-89-5 CAPLUS

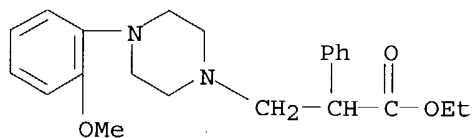
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-,
2-methylpropyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 132708-90-8 CAPLUS

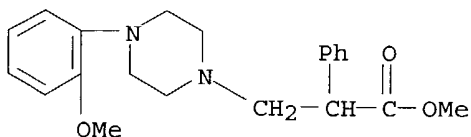
CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, ethyl
ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 132709-05-8 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl-, methyl
ester, dihydrochloride (9CI) (CA INDEX NAME)

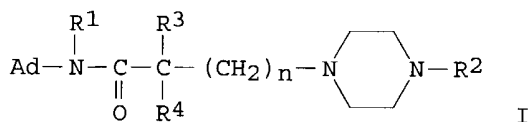


●2 HCl

10/049795

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:532219 CAPLUS
 DN 113:132219
 TI Preparation of piperazinylalkylcarboxylic acid adamantylamides as
 anxiolytics, antidepressants, and antipsychotics
 IN Abou-Gharbia, Magid A.; Yardley, John P.; Childers, Wayne E., Jr.; Cliffe,
 Ian A.
 PA American Home Products Corp., USA; John Wyeth and Brother Ltd.
 SO U.S., 4 pp. Cont.-in-part of U.S. Ser. No. 297,509, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4921958	A	19900501	US 1989-413407	19890927
	GB 2227018	A1	19900718	GB 1990-349	19900108
	GB 2227018	B2	19920520		
	DD 296921	A5	19911219	DD 1990-339954	19900420
	ZA 9003019	A	19911224	ZA 1990-3019	19900420
	ZA 9003020	A	19911224	ZA 1990-3020	19900420
	DD 297968	A5	19920130	DD 1990-339955	19900420
	US 5364849	A	19941115	US 1992-911996	19920710
	GB 2255976	A1	19921125	GB 1992-15425	19920720
	GB 2255976	B2	19921125		
	US 5382583	A	19950117	US 1992-998887	19921229
	US 5340812	A	19940823	US 1993-1428	19930107
	US 5420278	A	19950530	US 1994-248124	19940524
	US 5541326	A	19960730	US 1994-339000	19941114
PRAI	US 1989-297509	B2	19890113		
	GB 1989-9209	A	19890422		
	GB 1989-24323	A	19891028		
	US 1990-511150	B2	19900419		
	GB 1990-8925	A3	19900420		
	US 1991-748496	B1	19910822		
	US 1991-748497	B1	19910822		
	US 1991-756932	B1	19910909		
	US 1992-911996	A3	19920710		
	US 1992-998887	A3	19921229		
OS	MARPAT 113:132219				
GI					



AB Title amides I [Ad = 1- or 2-adamantyl, 3-noradamantyl; n = 1-5; R1 = H, alkyl, (substituted) Ph, CH2Ph; R2 = pyridinyl, pyrimidinyl, pyrazinyl, (substituted) Ph, CH2Ph; R3, R4 = H, Me, Ph, CH2Ph] were prepared. Thus, alkylation of 1-(2-methoxyphenyl)piperazine by 3-bromo-N-(1-adamantyl)propanamide in CH2Cl2 containing EtN(Me2CH)2, followed by workup, chromatog., and acidification gave I (Ad = 1-adamantyl, n = 1, R1 = R3 = R4 = H, R2 = 2-MeOC6H4) (II) as its di-HCl salt in 20% yield. II showed a 5-HT1A receptor affinity comparable to buspirone, and D2 dopaminergic

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affinity sufficient for antipsychotic utility. Two addnl. I were prepared, showing 5-HT1A activity but without significant D2 activity.

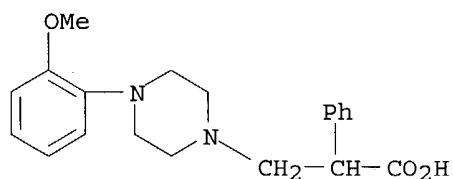
IT **129394-10-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of anxiolytics)

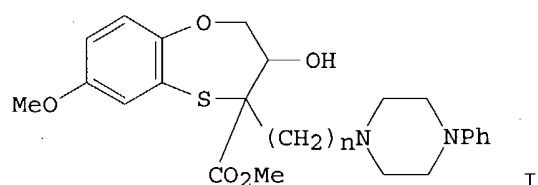
RN 129394-10-1 CAPLUS

CN 1-Piperazinepropanoic acid, 4-(2-methoxyphenyl)- α -phenyl- (9CI) (CA INDEX NAME)



10/049795

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:112411 CAPLUS
DN 108:112411
TI 1,5-Benzoxathiepin derivatives. II. Synthesis and serotonin
S2-receptor-blocking activity of aminoalkyl-substituted
3,4-dihydro-2H-1,5-benzoxathiepin-3-ols and related compounds
AU Sugihara, Hirosada; Mabuchi, Hiroshi; Hirata, Minoru; Imamoto, Tetsuji;
Kawamatsu, Yutaka
CS Cent. Res. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SO Chemical & Pharmaceutical Bulletin (1987), 35(5), 1930-52
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
OS CASREACT 108:112411
GI



AB Novel 1,5-benzoxathiepin derivs., e.g., I ($n = 3, 4, 5$), with an aminoalkyl group at the 2-, 3-, 4-position, were synthesized and evaluated for serotonin S2-receptor-blocking activity and adrenergic $\alpha 1$ -receptor-blocking activity. Me 4-aminoalkyl-3-hydroxy-3,4-dihydro-2H-1,5-benzoxathiepin-4-carboxylates showed significant S2-receptor-blocking activities. Structure-activity relationships, including the results of a conformational study and skeletal modifications, were examined. In the series of 1,5-benzoxathiepin, 1-benzoxepin and 1-benzothiepin derivs., Me cis-3-hydroxy-7-methoxy-4-[3-(4-phenyl-1-piperazinyl)propyl]-3,4-dihydro-2H-1,5-benzoxathiepin-4-carboxylate hydrochloride (CV-5197) showed the most potent and the most selective S2-receptor-blocking activity in the binding profile, and was chosen as a candidate for further pharmacol. evaluation.

IT 113272-89-2P 113272-90-5P 113272-91-6P
113272-92-7P

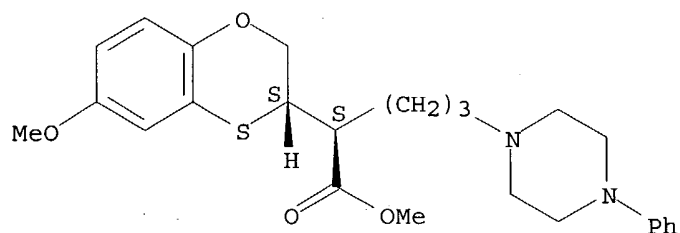
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 113272-89-2 CAPLUS

CN 1-Piperazinepentanoic acid, α -(2,3-dihydro-6-methoxy-1,4-benzoxathiin-3-yl)-4-phenyl-, methyl ester, (R*,R*)- (9CI) (CA INDEX NAME)

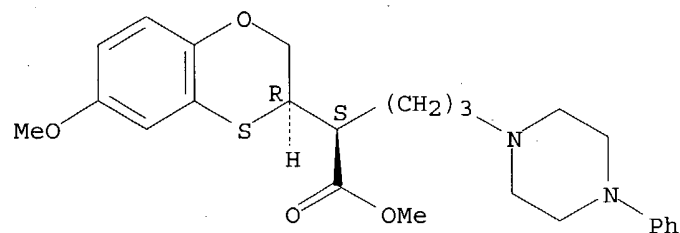
Relative stereochemistry.

10/049795



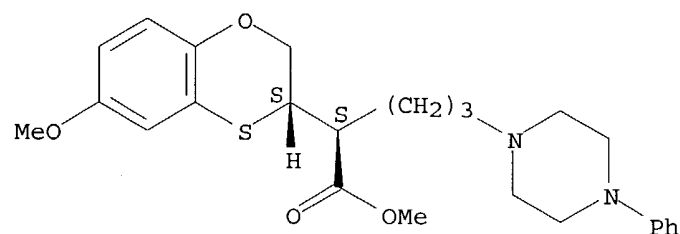
RN 113272-90-5 CAPLUS
CN 1-Piperazinepentanoic acid, α -(2,3-dihydro-6-methoxy-1,4-benzoxathiin-3-yl)-4-phenyl-, methyl ester, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 113272-91-6 CAPLUS
CN 1-Piperazinepentanoic acid, α -(2,3-dihydro-6-methoxy-1,4-benzoxathiin-3-yl)-4-phenyl-, methyl ester, monohydrochloride, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

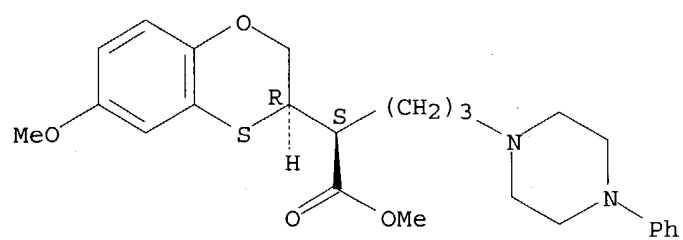


● HCl

RN 113272-92-7 CAPLUS
CN 1-Piperazinepentanoic acid, α -(2,3-dihydro-6-methoxy-1,4-benzoxathiin-3-yl)-4-phenyl-, methyl ester, monohydrochloride, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

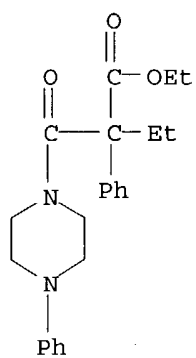
10/049795



● HCl

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1968:506663 CAPLUS
DN 69:106663
TI Analogs and derivatives of α -phenyl- α -ethylmalonic acid
N-(2-diethylaminoethyl)amide
AU Buttini, A.; Melandri, M. M.; Galimberti, P.
CS Schelabor S.p.A., Milan, Italy
SO Bollettino Chimico Farmaceutico (1968), 107(6), 362-9
CODEN: BCFAAI; ISSN: 0006-6648
DT Journal
LA Italian
AB A number of compds. related to Fenalamide $\text{RCOCPhEtCO}_2\text{Et}$ (I) ($\text{R} = \text{NHCH}_2\text{CH}_2\text{NET}_2$) were synthesized and their pharmacol. activities tested. Thus, to a mixture of 0.1 mole $\text{PhEtC(CO}_2\text{Et)COCl}$ and 0.1 mole Na_2CO_3 in 150 ml. C_6H_6 , 0.1 mole of the appropriate amine added with cooling, and the whole refluxed 4 hrs., gave the following I (R , b.p./mm., and m.p. HCl salt given): 4-methylpiperazino, 152-3°/0.2, 171-2°; 4-phenylpiperazino 205-6°/0.3, 181-3°; 4-benzylpiperazino, 206-8°/0.3, 192-4°; 4-(2-hydroxyethyl)piperazino, 198-9°/0.3, 153-4°; $\text{O(CH}_2)_2\text{O(CH}_2)_2\text{NET}_2$ (II), 183-4°/0.8, -; and $\text{O(CH}_2)_2\text{NETPh}$, 204-6°/0.8, -. To a solution of 0.1 mole MeONa in 200 ml. MeOH , 0.1 mole $\text{EtPhC(CO}_2\text{Et)}_2$ and 0.5 mole of the appropriate amine added and the mixture refluxed 8 hrs. gave the following $\text{EtCR}_1(\text{CONHR})_2$ (III) ($\text{R}_1 = \text{Ph}$) (IV) (R and b.p./mm. or m.p. given): $(\text{CH}_2)_2\text{NET}_2$ (IVa), 180-5°/0.5; $(\text{CH}_2)_2\text{NMe}_2$, 180-5°/0.7; $(\text{CH}_2)_3\text{NET}_2$, 170-3°/0.3; $(\text{CH}_2)_3\text{NMe}_2$, 180-5°/1; $(\text{CH}_2)_2\text{OH}$, 126-7°; $(\text{CH}_2)_3\text{OH}$, 94-5°; and $(\text{CH}_2)_4\text{Me}$, 200-4°/0.4. Similarly prepared from $\text{ZCH}_2\text{Cet(CO}_2\text{Et)}_2$ ($\text{Z} = \text{piperidino}$) were the following III ($\text{R}_1 = \text{piperidinomethyl}$) (R and b.p./mm. given): $(\text{CH}_2)_2\text{NET}_2$, 180-90°/0.8; $(\text{CH}_2)_3\text{NET}_2$, 185-95°/0.6; $(\text{CH}_2)_2\text{NMe}_2$, 177-80°/0.3; $(\text{CH}_2)_3\text{NMe}_2$, 200-10°/0.7; $(\text{CH}_2)_2\text{OH}$, 160-8°/0.8; $(\text{CH}_2)_3\text{OH}$, 200-10°/0.6; and $(\text{CH}_2)_4\text{Me}$, 200-5°/0.5. Finally, a solution of 0.1 mole $\text{EtCH(CO}_2\text{Et)}_2$, 0.11 mole paraformaldehyde, 0.1 mole pyrrolidine, and 500 ml. EtOH refluxed 6 hrs. gave $\text{QCH}_2\text{Cet(CO}_2\text{Et)}_2$ ($\text{Q} = \text{pyrrolidino}$), b1 115-20°, which allowed to react with an appropriate amine as reported for IV, gave the following III ($\text{R}_1 = \text{pyrrolidinomethyl}$) (R and b.p./mm. given): $(\text{CH}_2)_2\text{NET}_2$, 204-10°/0.9; and $(\text{CH}_2)_3\text{NET}_2$, 200-10°/0.8. II exhibited a high anticholinergic activity in vitro; IVa exhibited at 50 mg./kg. i.p. or at 180 mg./kg. per os a remarkable antitussive activity in rats.
IT 20389-21-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 20389-21-3 CAPLUS
CN 1-Piperazinepropionic acid, α -ethyl- β -oxo- α ,4-diphenyl-, ethyl ester (8CI) (CA INDEX NAME)

10/049795



10/049795

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1965:91011 CAPLUS
DN 62:91011
OREF 62:16272b-d
TI 1-(4-Aryl-5-hydroxypentyl)-4-arylpiperazines
PA UCB (Union Chimique-Chemische Bedrijven), Societe Anon.
SO 7 pp.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PRAI	GB		19630114		

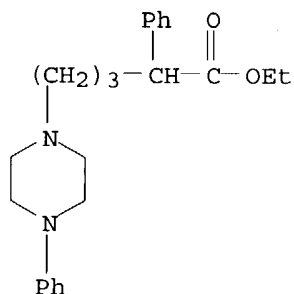
GI For diagram(s), see printed CA Issue.

AB Compds. of the general formula I are prepared and can be used in the treatment of neurotic disorders. Thus, a mixture of 10 ml. H₂O, 80 ml. H₂SO₄ (d. 1.83), and 39.2 g. 1-(4-phenyl-4-cyanobutyl)-4-phenylpiperazine-2HCl is heated 3 hrs. at 120°, 1 kg. EtOH is added dropwise as the H₂O is distilled, and the mixture is cooled and made alkaline with NaOH. The mixture is extracted with 250 ml. C₆H₆, the extract is concentrated, and the residue is treated with HCl(EtOH) to give 1-(4-phenyl-4-carbethoxybutyl)-4-phenylpiperazine-2HCl (II), m. 197-9°. II in H₂O is treated with 50 ml. 40% NaOH, the mixture is extracted with C₆H₆, the extract is evaporated to dryness, the residue is dissolved in 100 ml. ether, and a mixture of the solution and 1.5 g. LiAlH₄ in 125 ml. ether is refluxed 6 hrs. to give 13.5 g. 1-(4-phenyl-5-hydroxypentyl)-4-piperazine, m. 85-6° (ether). Also prepared are the following I (R, X, and m.p. 2HCl salt given): Me, MeO, 186-7° (Me₂CO); H, MeO, 180° (alc.-ether). Also prepared are p-MeC₆H₄CH(CO₂H)(CH₂)₃Cl (m. 75-6°) and p-MeC₆H₄CH(CH₂OH)(CH₂)₃Cl.

IT 2870-53-3, 1-Piperazinevaleric acid, α,4-diphenyl-, ethyl ester, dihydrochloride (preparation of)

RN 2870-53-3 CAPLUS

CN Valeric acid, 2-phenyl-5-(4-phenyl-1-piperazinyl)-, ethyl ester, dihydrochloride (8CI) (CA INDEX NAME)



● 2 HCl

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1963:448345 CAPLUS

DN 59:48345

OREF 59:8732a-c

TI New derivatives of N, N'-disubstituted piperazine having neurotropic properties

AU Morren, H.; Zivkovic, D.; Linz, R.; Strubbe, H.; Marchal, L.

CS Union Chim.-Chem. Bedrijven, Brussels

SO Industrie Chimique Belge (1963), 28, 123-34

CODEN: ICBEAJ; ISSN: 0019-9052

DT Journal

LA Unavailable

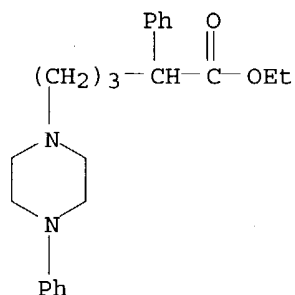
GI For diagram(s), see printed CA Issue.

AB Hydrochlorides of I were prepared by classical methods. R was H, lower alkyl, OMe, halogen in o, m, or p; R1 was H, Me, OMe, Cl, CF3 in o, m, or p; R2 was H, CN, CONH2, CONMe2, CO2Et, COMe, COEt, COPr, CH2NH2, CH2OH; and Z was (CH2)2-4, CH2CHMeCH2, CHMeCH2. The maximum neurotropic activity was found for I [R2 = CN, Z = (CH2)3] where R = halogen, Me, or MeO in para position and R1 = halogen, Me, or MeO in ortho position.

IT 2870-53-3, 1-Piperazinevaleric acid, α ,4-diphenyl-, ethyl ester, dihydrochloride 96457-75-9, 1-Piperazinevaleric acid, 4-(o-methoxyphenyl)- α -phenyl-, ethyl ester, dihydrochloride (preparation of)

RN 2870-53-3 CAPLUS

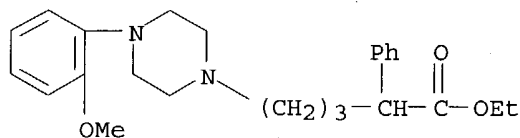
CN Valeric acid, 2-phenyl-5-(4-phenyl-1-piperazinyl)-, ethyl ester, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

RN 96457-75-9 CAPLUS

CN 1-Piperazinevaleric acid, 4-(o-methoxyphenyl)- α -phenyl-, ethyl ester, dihydrochloride (7CI) (CA INDEX NAME)



●2 HCl

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

100.76

257.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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2 L3

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10/049795

L5 ANSWER 1 OF 2 CAOLD COPYRIGHT 2004 ACS on STN

AN CA62:16272b CAOLD

TI 1-(4-aryl-5-hydroxypentyl)-4-arylpiperazines

PA UCB (Union Chimique-Chemische Bedrijven), S.A.

DT Patent

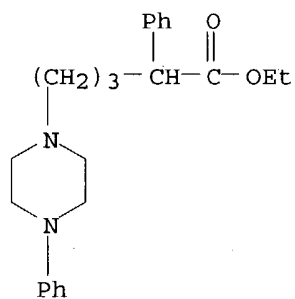
PATENT NO.	KIND	DATE
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PI BE 642084

IT 2870-53-3

RN 2870-53-3 CAOLD

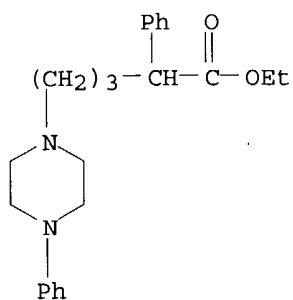
CN Valeric acid, 2-phenyl-5-(4-phenyl-1-piperazinyl)-, ethyl ester,
dihydrochloride (8CI) (CA INDEX NAME)



● 2 HCl

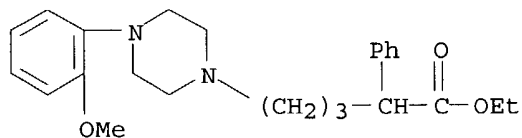
10/049795

L5 ANSWER 2 OF 2 CAOLD COPYRIGHT 2004 ACS on STN
AN CA59:8732a CAOLD
TI derivs. of N,N'-disubstituted piperazine having neurotropic properties
AU Morren, Henri; Zivkovic, D.; Linz, R.; Strubbe, H.; Marchal, L.
IT 2870-53-3 96457-75-9
RN 2870-53-3 CAOLD
CN Valeric acid, 2-phenyl-5-(4-phenyl-1-piperazinyl)-, ethyl ester, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

RN 96457-75-9 CAOLD
CN 1-Piperazinevaleric acid, 4-(o-methoxyphenyl)- α -phenyl-, ethyl ester, dihydrochloride (7CI) (CA INDEX NAME)



●2 HCl